Mid-term results after endovascular stent-graft placement due to penetrating atherosclerotic ulcers of the thoracic aorta

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Abstract

Background: To determine mid-term durability of endovascular stent-graft placement in patients with penetrating atherosclerotic ulcers (PAU) involving the thoracic aorta and to identify risk factors for death as well as early and late cardiovascular events. Methods: From 1997 to 2006, 27 patients (mean age 66 yrs) presented with PAU (rupture n = 7). Mean numeric EuroScore was 11 and mean logistic EuroScore was 35. Median follow-up was 42 (10—86) months, being complete in all patients. Outcome variables included death and occurrence of early and late cardiovascular events. Results: In-hospital mortality was 11%. Primary success rate was 100%. Actuarial survival rates at 1, 3 and 5 years were 93%, 78% and 70%, respectively. Hemodynamic instability (HR 2.5, 2.1—3.9; p = 0.034) as well as logistic EuroScore (HR 2.8, 2.4—4.3; p = 0.019) was identified as independent predictor of early and late cardiovascular events. Conclusions: Endovascular stent-graft placement in patients with PAU is an effective palliation for a life-threatening sign of a severe systemic process. Hemodynamic instability at referral and a high preoperative risk score predict adverse outcome. During mid-term follow-up, patients are mainly limited by sequelae of their underlying disease.

Keywords: Penetrating; Atherosclerotic ulcer (PAU); Arch rerouting; Endovascular stent-graft

1. Introduction

Penetrating atherosclerotic ulcers have recently been defined as a distinct entity of acute aortic syndromes [1] gaining increasing importance by improved diagnostic means and by sensibilization of the surgical community to the pathology itself. Being the result of an advanced obliterative atherosclerotic systemic process, penetrating atherosclerotic ulcers (PAU) may also be associated with other severe manifestations of the underlying disease. The natural history, especially of symptomatic PAU is dismal [2,3]. Superiority of endovascular stent-graft placement as compared with medical or conventional surgical therapy has been proven for various indications of acute pathologies of the thoracic aorta [4—9].

The aim of this study was to determine mid-term durability of endovascular stent-graft placement in patients with penetrating atherosclerotic ulcers involving the thoracic aorta and to identify risk factors for death as well as early and late cardiovascular events.

2. Patients and methods

From 1997 to 2006, 27 patients (mean age 66 yrs) presented with PAU (rupture n = 7). Patient demographics are shown in Table 1. All patients underwent risk stratification according to EuroScore guidelines [10]. EuroScore is known as a widespread preoperative risk stratification system encompassing demographic, cardiac-related as well as surgery-related variables. Both, additive and logistic values were collected as logistic EuroScore has been reported to be a better risk predictor in high-risk patients [11].

2.1. Preoperative evaluation, landing zones and surgical approach

Preoperative evaluation was by multislice CT scans in order to exclude major occlusive disease of the supraaortic branches as well as of the aortoiliac axis for later arterial access for stent-graft insertion. Furthermore, these CT scans were used as a tool to predict the required length of landing zones.
zones. In patients requiring proximal landing zone extension, an autologous or alloplastic approach, according to the required length, was chosen. The original methods of the autologous approach, double transposition of the supraaortic branches, as well as of the alloplastic approach (total arch rerouting) have been described in detail previously [12,13].

2.2. Stent-graft systems used

Four different commercially available stent-graft systems were used. The Excluder stent-graft (WL GORE, Flagstaff, AZ), and after having been modified, the TAG stent-graft was used in 14 patients. The Talent endovascular stent-graft (Medtronic, Santa Rosa, CA) was used in nine patients. The Relay stent-graft (Bolton Medical, Sunrise, FA) was used in two patients. Finally, the Evita stent-graft (Jotec, Hechingen, Germany) was used in further two patients. For all systems, the diameter of the stent-graft was calculated from the largest diameter of the proximal or distal neck and an oversizing factor of 10–20% was added.

2.3. Stent-graft placement

Stent-graft placement was performed during general anesthesia. Due to the underlying obliterative arteriopathy, in 40% of patients, access had to be gained via the common iliac artery. A 9 mm Dacron prosthesis was sutured to the native vessel in an end-to-side fashion and stent-graft placement was performed via the prosthesis. At the end of the procedure, the Dacron prosthesis was ligated and additionally oversewn at the level of the native vessel. In the remaining patients, access was gained via the common femoral artery. Stent-graft deployment was routinely performed under hypotonic conditions (60 mmHg systolic pressure).

2.4. Imaging studies evaluation

All patients were subjected to a strict follow-up protocol encompassing spiral contrast CT or magnetic resonance angiography before discharge, at 3, 6, 12 months and annually thereafter.

2.5. Definition of endpoints

Death was defined as in-hospital death or death during follow-up. Early and late cardiovascular events were defined as any occurrence of stroke, myocardial infarction as well as any requirement for cardiac or vascular operations or interventions.

2.6. Statistical analysis

Continuous variables are expressed as means ± SD. Categorical variables are expressed as percentages. To determine risk factors a stepwise logistic regression analysis was performed. The entrance level for multivariate analysis was a p value of below 0.05 within univariate analysis. Statistical analysis was performed with SPSS 11.0 statistical software (SPSS, Inc., Chicago, IL).

3. Results

3.1. Locations and extensions of lesions

Locations of PAU are depicted in Fig. 1. The majority of lesions were located in the proximal third (n = 7) and in the mid third (n = 11) of the descending aorta. The distal descending aorta was affected in four patients. The remaining patients had their lesions located either in the mid arch (n = 2) or in the distal arch (n = 3). Furthermore, the majority of the lesions were limited to the very segment

<table>
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<tr>
<th>Demographics and clinical risk factors</th>
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<tr>
<td>Age (yrs) 66 (37–84)</td>
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<tr>
<td>Male (%) 82</td>
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<tr>
<td>Additive EuroScore 11 (5–18)</td>
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<td>Logistic EuroScore 34 (5–80)</td>
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<tr>
<td>Chronic obstructive pulmonary disease (%) 40</td>
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<tr>
<td>Previous myocardial infarction (%) 40</td>
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<td>Peripheral arterial occlusive disease (%) 60</td>
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<td>Renal insufficiency (%) 26</td>
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<tr>
<td>Diabetes mellitus (%) 11</td>
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<td>Previous cerebrovascular events (%) 15</td>
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<td>Previous heart surgery (%) 15</td>
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<td>Suitable for conventional surgery (%) 15</td>
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Chronic obstructive pulmonary disease—defined as long-term use of bronchodilators or steroids for lung disease.
Previous myocardial infarction—defined as enzyme infarction with morphological or functional correlate in coronary angiography or echocardiography.
Peripheral arterial occlusive disease—defined as one or more of claudication, carotid occlusion or >50% stenosis, planned intervention on the abdominal aorta, limb arteries or carotids.
Renal insufficiency—defined as serum creatinine ≥2 mg/dl in repeated measurements.
Diabetes mellitus—defined as serum hyperglycemia requiring oral sulfonylurea intake or insulin substitution.
Previous cerebrovascular events—defined as previous minor or major neurologic adverse events irrespective of origin with and without remaining morphological or functional correlate.
Previous heart surgery—defined as open-heart surgery irrespective of indication.
Suitable for conventional surgery—defined as suitability for conventional thoracic aortic surgery according to preoperative risk stratification.

Fig. 1. Locations of PAU.
of the initial location. Merely in three patients progression in other thoracic aortic segments could be seen. Fig. 2 shows a CT scan in a patient with multiple PAU. Fig. 3 depicts the axial images at different heights in the same patient.

3.2. Surgical procedure

Four elective patients underwent surgical extension of the proximal landing zone before stent-graft placement. Two patients underwent autologous double transposition and two patients underwent total arch rerouting. All patients recovered uneventfully without any signs of transient or permanent neurologic injury after rerouting of the suprarenal branches. Fig. 4 shows the completion CT scan post double transposition.

3.3. Stent-graft placement and clinical outcome

Primary success rate was 100%. Fig. 5 depicts the intraoperative situs at the level of the right common iliac artery with a 9 mm Dacron graft sewn onto the native vessel for easier stent-graft insertion. Mean number of stent-grafts used was 1.3. Three early in-hospital deaths had to be observed. One patient after stent-graft placement due to an aorto-esophageal fistula sustained fatal bleeding 4 days after the initial procedure. Another patient undergoing stent-graft placement under emergency conditions died due to acute mesenteric ischemia 2 weeks after the initial procedure. The final patient died 4 months after emergency stent-graft placement due to multi-organ failure. The remaining patients experienced an uneventful clinical course. Fig. 6 depicts a CT scan post stent-graft.

3.4. Follow-up period

The mean follow-up period was 42 months (range 10–86 months). Two late type Ib endoleaks had to be observed. One of these patients underwent open thoracoabdominal repair due to the inability of a further endovascular approach. Four late deaths occurred during follow-up (myocardial infarction $n=3$, fatal stroke $n=1$). Furthermore, in four patients, seven cardiac or vascular operations or interventions, respectively, had to be performed due to progression of the underlying obliterative atherosclerotic disease. Actuarial survival rates at 1, 3 and 5 years were 93%, 78% and 70%, respectively.

3.5. Cox proportional hazards model

Hemodynamic instability at referral (HR = 2.5, $p = 0.034$) and logistic EuroScore (HR = 2.8, $p = 0.019$) were the only independent predictors of death as well as early and late adverse cardiovascular events. Interestingly, age (HR = 1.0, $p = 0.488$) did not turn out to be an independent predictor.
4. Comment

Endovascular stent-graft placement in patients with PAU is an effective palliation for a life-threatening sign of a severe systemic process. Hemodynamic instability at referral and a high preoperative risk score predict adverse outcome. During mid-term follow-up, patients are mainly limited by sequelae of their underlying disease.

A variety of acute and chronic aortic pathologies are now being detected by improved diagnostic means. Therefore, PAU has gained increasing attention of the surgical community. In contrast to the decision-making in patients with atherosclerotic thoracic aortic aneurysms, the maximum diameter of PAU plays a minor role. Morphology, and if applicable and traceable, progression of the lesion are the cornerstones of decision-making besides clinical symptoms or already sustained rupture [1—3]. Therefore general guidelines for treatment have yet to be established by a multidisciplinary working group. Furthermore, the location of the lesion plays an important role. The majority of lesions in this series were located either in the proximal third or in the mid-third of the descending aorta. Therefore, the length of the landing zone was deemed sufficient without any need for surgical landing zone extension. If more distal segments of the thoracic aorta are involved, other important factors have to be considered. In contrast to atherosclerotic thoracic aortic aneurysms, where intercostal arteries do not show any antegrade flow pattern due to the parietal thrombus within the aneurysmal sac, these vessels are likely to be patent in patients with PAU. Therefore the risk of paraplegia when covering the distal third of the thoracic aorta or the thoracoabdominal transition may be higher. Fortunately, we did not observe spinal ischemia in this series. Additionally, experimental and clinical data support the hypothesis, that spinal ischemia is mainly induced by prolonged periods of systemic hypotension and not by the number of patent intercostals arteries [14,15]. Finally, cerebrospinal fluid drainage during and within the first 72 h after stent-graft placement may serve as a valuable adjunct in avoiding this serious adverse event [16].

In case of location of PAU within the aortic arch, vascular surgical approaches to maintain cerebral perfusion are warranted to enable safe and effective endovascular repair. Depending on the extent of lesions within the arch, autologous approaches or approaches using alloplastic graft material to maintain cerebral perfusion may be used [7,9,12,13,17]. These supraaortic transpositions broaden the accessible range of lesions and do not expose patients at substantially elevated surgical risk.

The time interval from referral to treatment is crucial. Our setting implies an emergency room, where a CT scan can be performed routinely, and immediately thereafter treatment can be initiated. Therefore the mean interval in our setting is short, being 90 min. Despite a primary technical success rate of 100%, in-hospital mortality was 11%. All three patients who died underwent stent-graft placement under emergency conditions having already sustained rupture. One patient sustained a fatal bleed 4 days after the initial procedure with the primary indication of an aorto-esophageal fistula. It has to be stated that this patient had undergone heart transplantation 13 years ago and the general condition did not allow any conventional approach. On the other hand the indication remains open for discussion as inserting alloplastic material in a potentially infected area may be regarded merely as a bail-out approach and not as a definite solution of a potentially unsolvable problem. The remaining two patients underwent stent-graft placement in a state of prolonged systemic hypotension due to rupture with consecutive hemodynamic compromise. In one patient this situation being associated with substantial pressor support led to non-occlusive mesenteric ischemia with all its
deleterious consequences. In the other patient the emergency condition shipwrecked the already weak physiological balance resulting in multi-organ failure and consequently, death.

The rate of endoleak formation during follow-up is acceptably low. This might be related to the fact that the majority of lesions are well defined and not as extensive as in atherosclerotic thoracic aortic aneurysms. Therefore the majority of landing zones are well defined and due to the obliterator origin of the pathology itself, dilation of initially normally calibrated segments is unlikely.

Interestingly, the number of secondary cardiac or vascular operations or interventions has been high and is definitely higher when compared with the number observed after stent-graft placement for other thoracic aortic pathologies. This might also be related to the underlying obliterator atherosclerotic disease as PAU is rarely the primary manifestation of the disease itself. Therefore the majority of these patients are in an advanced state of systemic obliterator atherosclerosis and are therefore, despite secondary prevention, at high risk of developing symptomatic atherosclerotic lesions in other vascular beds.

Hemodynamic instability at referral as well as logistic EuroScore was the only independent predictors of death as well as early and late adverse cardiovascular events. This seems reasonable when reflecting on the issue that the majority of these patients are in advanced stage of systemic and cardiac hemodynamic instability, leading to hyperbaric and substantial inotropic and pressure support and consequently, due to the diminished physiological reserve, in irreversible end-organ failure. Logistic EuroScore as compared with numeric EuroScore has been reported to be a better risk predictor in high-risk patients

4.1. Limitations of the study

This series represents a single center limited experience. We cannot provide a medical or surgical control group particularly in patients undergoing stent-graft placement in an elective setting where predominantly the morphology of PAU was the reason for treatment. Finally it remains speculative, due to the severe underlying disease if treatment of PAU, especially in the elective setting, has a beneficial impact on long-term prognosis.

Summarizing, endovascular stent-graft placement in patients with PAU is an effective palliation for a life-threatening sign of a severe systemic process. Hemodynamic instability at referral and a high preoperative risk score predict adverse outcome. During mid-term follow-up, patients are mainly limited by sequelae of their underlying disease.

References


Appendix A. Conference discussion

Dr S. Schueler (Newcastle Upon Tyne, UK): Can you just tell us who is actually practically doing the procedure? Is it all in the hands of the surgeons or are interventional radiologists involved, or what is your concept of approaching these patients in general?

Dr Czerny: In our center it is a team approach, so historically interventional radiologists and surgeons are seeing the patients together, do the decision-making together, and treat the patients together.

Dr Schueler: But what actually are you doing as surgeons? Are you placing the stent or is the stent placed by the radiologist and you just do the cut down?

Dr Czerny: The stent is placed by the interventional radiologist, however, you are the clinical manager of the case, and I think this is the important issue.
Dr H. Shennib (Phoenix, AZ): This is one of the most complex and challenging group of patients to decide who to operate on or who not, shaggy aortas, and the biggest manifestation that they come up with is atheroembolic disease, and there is always a question about what is the limit? I mean, you look at the aorta and you see all those atherosclerotic ulcers and plaques, and some of those patients may have major symptoms, some of them have minor. When they have stroke or something or blue toes, then you know that you have to do something, but then you see a population of patients with the shaggy aortas and you are really not sure what the limit is, particularly when it is a proximal arch disease and you know that you are now about to move into not only doing endovascular procedures but also doing debranching and so on.

So I want some sort of an idea from you: what is your limit, where do you stop, and how do you choose your patients?

Dr Czerny: Actually I think it remains a very individual decision from case to case, and actually the issue is that there are no clear indications or no clear guidelines when to treat an ulcer or not. I think that the decision which patient is the patient to treat or not remains a very individual and maybe even subjective decision. And of course you have to think about the general status, and if you make something better for a long-term prognosis when treating these patients, this is a crucial issue.

Dr B. Zipfel (Berlin, Germany): We have quite a bit of experience with this also. And one thing I am wondering, you have the distribution. You had no access in the thoracoabdominal region close to the thoracoabdominal vessels. You had quite a few, which are very difficult to treat endovascularly. Do you have any explanation for this?

Dr Czerny: Actually not.

Dr D. Veerasingam (Galway, Ireland): Going on from the earlier comment, especially when you have disease which is going into the hemiarch and the ascending arch, what would be a good approach? Would it be like a stent followed by proximal graft replacement or just graft replacement first and then a stent later?

Dr Czerny: Our concept is always to re-route initially and then stenting in a second step.

Dr A. Haverich (Hannover, Germany): I would be interested to know the following: during the same period where you treated those patients interventionaly, how many patients were there where intervention was not possible due to either kinking of the aorta or peripheral vascular disease that access was too difficult? And what did you do with those patients? Did you take them for routine surgery or did you leave them alone and treat them conservatively?

Dr Czerny: There is hardly ever a patient we have refused these procedures due to access problems. Within the last year I can remember one patient where we failed, but we left it because actually all these patients we offer this treatment modality are not deemed suitable for any kind of conventional repair.